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Dear Mike:

Thank you for your letter of January 12, 1982. To take care of business first, I have asked that an ASP 66 form be sent to you this week and I gather that it has already gone to you in the mail. We look forward to seeing you in February. I myself will be out of town the third week in February, but I will leave word that you're expected and you will be very welcome to arrive at any time. As far as apartments are concerned, the only apartment that I know of at the moment is one next door to the apartment of Larry Donehower, another postdoctoral fellow. However, new arrivals generally find that it's not difficult to obtain housing after a few days of search and you will find many people here prepared to give you perhaps more advice than you would like about how to find a suitable place to live.

The results you've obtained with the SV40 system are obviously of extreme interest to us and I look forward to hearing more about those results when you arrive. Naturally, the kinds of things you were doing have interest to us from the point of view of retrovirus induced tumors. Some of the experiments you proposed in the lymphoma system have been proposed by another incoming postdoctoral fellow, Carol Nottenberg, who will be working on avian lymphomas beginning sometime this spring. However, there are several other contexts in which the kind of approach you might like to take might be appropriate. For example, we have recently found in mammary tumors induced by the mouse mammary tumor virus that the same region of the host genome is occupied by proviral DNA in about 20% of tumors. As yet, however, we have been unable to identify transcriptional units that are affected by these insertions. In addition, Dave Westaway, whom you may remember from St. Mary's in London, has been looking at nephroblastomas induced by the virus MAV2 Although MAV2 inserts its DNA in c-myc when it induces lumphoid leukosis, it does not cause insertions in c-myc when it induces nephroblastomas. In all of these cases, of course, it's difficult to know whether a gene whose expression is enhanced exhibits changes that are a consequence or a cause of the transformed state. You might consider the possibility of looking in lymphomas that have been induced by SV40. These tumors which have been produced by pathologists at Harvard have never been well studied at the molecular level and they might provide some interesting comparisons with your previous work and with the work currently emerging from the study of retroviruses. We have been exploring, in so far a rather superficial way, the issue of gene activation in human tumors. I agree control tissue is difficult in this situation as you might have noticed from the recent

article in Nature from Gallo and Aaronson. We have been unable to obtain cell transformation in the Weinberg-Cooper type of assay using NIH 3T3 cells and we have only done very small amount of work looking for gene activation with probes for known oncogenes. However, the kinds of experiment you suggest using selected cDNA might be worth thinking about.

I look forward to your arrival and hope we can explore these issues in more detail after you arrive.

Yours sincerely,

Harold E. Varmus, M.D.
Professor

HEV/jm